

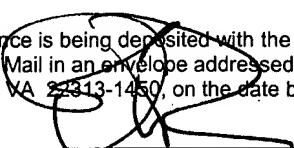


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November 5, 2004

Date


David L. Parker

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Michael C. MacLeod, Sara S. Gaddis and C.
Marcelo Aldaz

Serial No.: 09/840,722

Filed: April 23, 2001

For: COMBINATORIAL
OLIGONUCLEOTIDE PCR: A METHOD
FOR RAPID, GLOBAL EXPRESSION
ANALYSIS

Group Art Unit: 1634

Examiner: J. Taylor

Atty. Dkt. No.: UTSC:607USC1/DLP

BRIEF ON APPEAL

MS Appeal Brief

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CLAIMS APPENDIX (Tab 1)

EVIDENCE APPENDIX (Tab 2)

Exhibit A – Senapathy US 5,994,058

Exhibit B – Silver US 5,104,792



Sir:

Appellants hereby submit an original and three copies of this Brief on Appeal to the Board of Patent Appeals and Interferences in response to the final Office Action dated February 5, 2004 (the "Action"). The Notice of Appeal was filed on May 3, 2004 and received in the PTO on May 6, 2004, making the present appeal brief due on July 6, 2004.

A request for a four-month extension of time to respond is included herewith along with the required fee. This extension will bring the due date to November 6, 2004, which is within the statutory period. Should such request or fee be deficient or absent, consider this paragraph such a request and authorization to withdraw the appropriate fee under 37 C.F.R. §§ 1.16 to 1.21 from Fulbright & Jaworski L.L.P. Account No.: 50-1212/UTSC:607USC1.

The fee for filing this Appeal Brief is \$165 and is enclosed herewith, along with the \$765 fee for the extension of time. Please date stamp and return the attached postcard as evidence of receipt.

I. REAL PARTY IN INTEREST

The real parties in interest is The Board of Regents, The University of Texas System and its exclusive licensee Capitol Genomics, Inc.

II. RELATED APPEALS AND INTERFERENCES

There are no currently pending related appeals or interferences.

III. STATUS OF THE CLAIMS

The present application was filed with claims 1-84. Subsequently, on September 26, 2001, a preliminary amendment was filed whereby claims 1, 2, 5-19, 22, 30-35 and 77-84 were canceled, various claims were amended and new claims 85-89 were added. All of the claims

except claims 87-89 have been allowed. The present appeal is solely of the rejection of claims 87-89. A copy of the pending claims is attached Claims Appendix 1.

IV. STATUS OF AMENDMENTS

An amendment sought after final was not entered.

V. SUMMARY OF THE CLAIMED SUBJECT MATTER

The invention of the appealed claims concerns, in the context of claim 87, a pair of primer molecules wherein both members of the pair comprise (a) a predetermined 5' sequence that incorporates a sequence that anneals to a predetermined linker sequence and (b) a random 3' terminal specificity region of from 3 to 8 nucleotides in length, the specificity region defined as one of all possible sequence combinations of A, T, G and C. See page 21, lines 1-25. Claim 88 is directed to a population of the foregoing paired primer molecules and claim 89 concerns one member of the population. *Id.*

It is of particular note that with respect to the population of primers of claim 88, the population of primer molecules having specificity regions collectively reflecting all possible sequence combinations of A, T, G and C. See, e.g., Page 21, lines 4-9.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

Whether the subject matter of claims 87-89 are anticipated by or obvious over Senapathy *et al.*, US 5,994,058 (“Senapathy”; Exhibit A); and

Whether the subject matter of claims 87-89 are anticipated by or obvious over Silver *et al.*, US 5,104,792 (“Silver”; Exhibit B).

VII. ARGUMENT

A. Rejection of Claims 87-89 Under Section 102(a)/103 over Senapathy

1. Summary of the Rejection

The Action takes the position that the subject matter of claims 87-89 are anticipated or obvious over the Senapathy '058 patent. The examiner relies primarily on Figure 1 and specifically admits that “[a]dmitedly, this author does not teach that the primer will anneal to a linker sequence. Office Action of 3/12/03, paper 11, where the reference was first cited. However, the Examiner concludes that the language of the claims, “that is prepared to incorporate a sequence that anneals to a predetermined linker sequence,” is merely an intended use and thus must be disregarded.

2. Appellants' Remarks

a) *Substantial evidence required to uphold the Examiner's position*

As an initial matter, Appellant notes that findings of fact and conclusions of law by the U.S. Patent and Trademark Office must be made in accordance with the Administrative Procedure Act, 5 U.S.C. § 706(A), (E), 1994. *Dickinson v. Zurko*, 527 U.S. 150, 158 (1999). Moreover, the Federal Circuit has held that findings of fact by the Board of Patent Appeals and Interferences must be supported by “substantial evidence” within the record. *In re Gartside*, 203 F.3d 1305, 1315 (Fed. Cir. 2000). In *Gartside*, the Federal Circuit stated that “the ‘substantial evidence’ standard asks whether a reasonable fact finder could have arrived at the agency’s decision.” *Id.* at 1312.

Accordingly, an Examiner’s position on Appeal must be supported by “substantial evidence” within the record in order to be upheld by the Board of Patent Appeals and Interferences.

b) The standard for obviousness

In order to establish a *prima facie* case of obviousness, three basic criteria must be met:

(1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference (or references when combined) must teach or suggest all the claim limitations.

Manual of Patent Examining Procedure (M.P.E.P.) § 2142. Moreover, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on the Applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991). When "the motivation to combine the teachings of the references is not immediately apparent, it is the duty of the examiner to explain why the combination of the teachings is proper." M.P.E.P. § 2142.

c) Appellants' Argument

(1) Claims 87-89

In response, it is Appellants position that no proper *prima facie* rejection has been set forth by the Examiner. Applicants would first note that the claims are directed to primers having a 3' random specificity region and a 5' region that incorporate a sequence "that anneals to a predetermined linker sequence."

The Senapathy patent appears to disclose in Figures 1 through 3, the concept of "genome walking with a known first primer and a partly fixed second primer." Similarly, Figure 4 refers to the use of the "same set of partly fixed second primers" all working from a known primer which does not appear to have "unfixed" regions. Thus, these embodiments appear to be distinct from the invention of claim 87-89 which require that *both* members of the primer pairs incorporate random sequences in their specificity regions. The Examiner was unable to point to

any teaching in Senapathy that discloses primer pairs wherein both members of the pair incorporate random sequences in their specificity region.

With respect to the Examiner's contention that the claim language "that incorporates a sequence that anneals to a predetermined linker sequence" is merely an intended use limitation, Applicants again point out that this language presents a positive structural feature and simply cannot be said to be an intended use – it uses the language "that incorporates," it does *not* merely say "that may be used to bind" or "may be capable of binding" some other such variation. To anticipate such "that incorporates" language, the Examiner must demonstrate prior art that actually shows a primer that incorporates a sequence that binds to a linker. This has not been done. In any event, the claims now refer to a primer pair, wherein each member of the pair incorporates a sequence that binds to a *different* linker sequence, and are thus still further removed from the prior art.

(2) Claim 88

Claim 88 is to be considered separately patentable with respect to the rejection over Senapathy. That claim makes reference to the population of primer molecules having specificity regions collectively reflecting all possible sequence combinations of A, T, G and C.. The Examiner has failed to point to any such teaching in Senapathy that are relied upon for this concept.

B. Rejection of Claims 87-89 Under Section 102(a)/103 over Silver

1. *Summary of the Rejection*

The Action takes the position that the subject matter of claims 87-89 are anticipated or obvious over the Silver '792 patent. The examiner relies primarily on Figure 1 and specifically admits that "[a]dmitedly, these authors do not teach that their primer will anneal to a linker sequence. Office Action of 3/12/03; paper 11, where the reference was first cited:

However, the Examiner concludes that the language of the claims, “that is prepared to incorporate a sequence that anneals to a predetermined linker sequence,” is merely an intended use and thus must be disregarded. The Action further refers to col. 3, lines 55-57 of Silver and argues that the sequence 5’-GACTCNNNN-3’ will, if provided a linker sequence of 5’-XXXXGAGTC-3’, anneal thereto. Notably, the Action fails to direct us to a teaching of such a linker sequence.

2. *Appellant’s Remarks*

a) *Claims 87-89*

We respectfully disagree for the same reasons set forth above with respect to Senapathy, which are incorporated herein by reference. Furthermore, it is noted that the primers of Silver that contain random specificity regions are shown *not* to have 5’ regions that bind their template. For example, the Silver patent clearly discloses in Figure 1 that the region of *its* primers that is located 5’ of the random sequence *does not* bind to the template. It is not until the Silver prepares a primer that does *not* incorporate a random sequence that it teaches the use of a known sequence that binds to the template. See, for example, bottom of Figure 1 as compared to the first two depictions at the top of Figure 1.

The Action’s reference to col. 3, lines 55-57 of Silver, and its argument that the sequence 5’-GACTCNNNN-3’ will, if provided a linker sequence of 5’-XXXXGAGTC-3’, anneal thereto, is already commented upon above. This argument is unavailing as the Action fails to direct us to a teaching or suggestion of a linker that incorporate such a sequence. On the contrary, Silver teaches against such an embodiment since, as explained in the foregoing paragraph, the 5’ regions of its primers that have random sequences at their 3’ end do not bind to the template – only those primers that do not have random 3’ sequence bind to the template.

Indeed, the Action relies upon the 5'-GACTCNNNN-3' of Silver, but admittedly fails to demonstrate that the complement of such sequence is found in any known linker. Even if it is the case that the claim element (a) recites an intended use, it *also* recites a positive structural feature that must be taken into account.

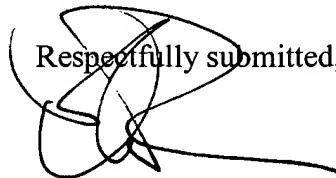
b) ***Claim 88***

Claim 88 is to be considered separately patentable with respect to the rejection over Silver as well. That claim makes reference to the population of primer molecules having specificity regions collectively reflecting all possible sequence combinations of A, T, G and C.. The Examiner has failed to point to any such teaching in Silver that teaches or suggest this concept.

IX. CONCLUSION

Appellants have provided arguments that overcome the pending rejections. Appellants respectfully submit that the Office Action's conclusions that the claims should be rejected are unwarranted. It is therefore requested that the Board overturn the Action's rejections.

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Respectfully submitted,

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Date: November 5, 2004

CLAIMS APPENDIX

87. A pair of primer molecules wherein both members of the pair comprise (a) a predetermined 5' sequence that incorporates a sequence that anneals to a predetermined linker sequence and (b) a random 3' terminal specificity region of from 3 to 8 nucleotides in length, the specificity region defined as one of all possible sequence combinations of A, T, G and C.
88. A population of paired primer molecules, the primer molecule pairs having (a) a predetermined 5' sequence that incorporates a sequence that anneals to a predetermined linker sequence and (b) a random 3' terminal specificity region of from 3 to 8 nucleotides in length, the population of primer molecules having specificity regions collectively reflecting all possible sequence combinations of A, T, G and C.
89. A primer molecule pair selected from the population of claim 88.

EVIDENCE APPENDIX

Exhibit A – Senapathy US 5,994,058

Exhibit B – Silver US 5,104,792